Genome sequencing of mouse induced pluripotent stem cells reveals retroelement stability and infrequent DNA rearrangement during reprogramming.

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Public Summary:
The biomedical utility of induced pluripotent stem cells (iPSCs) will be diminished if most iPSC lines harbor deleterious genetic mutations. Recent microarray studies have shown that human iPSCs carry elevated levels of DNA copy number variation compared with those in embryonic stem cells, suggesting that these and other classes of genomic structural variation (SV), including inversions, smaller duplications and deletions, complex rearrangements, and retroelement transpositions, may frequently arise as a consequence of reprogramming. Here we employ whole-genome paired-end DNA sequencing and sensitive mapping algorithms to identify all classes of SV in three fully pluripotent mouse iPSC lines. Despite the improved scope and resolution of this study, we find few spontaneous mutations per line (one or two) and no evidence for endogenous retroelement transposition. These results show that genome stability can persist throughout reprogramming, and argue that it is possible to generate iPSCs lacking gene-disrupting mutations using current reprogramming methods.

Scientific Abstract:
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